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Published
With international search report.

(54) Title: CNRE BINDING FACTORS AND USES THEREOF

(57) Abstract

The invention pertains to nucleic acids encoding CNRE-binding polypeptides, including fragments and biologically functional variants thereof. The invention also pertains to therapeutics and diagnostics involving the foregoing proteins and genes and agents that bind the foregoing proteins and genes.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/08502

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/185.1; 435/6, 320.1, 325, 375; 530/300, 350; 514/2, 44; 536/23.1, 23.5, 24.31, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, STN, GENBANK

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97/35018 A1 (NEW YORK UNIVERSITY) 25 September 1997, pages 83-84, see nucleotides 1187-1805 of SEQ. ID. NO: 1.	1 and 4
A	BARRETT et al. Identification of a Negative Regulatory Element Involved in Tissue-specific Expression of Mouse Renin Genes. Proceedings of the National Academy of Science, USA. February 1992, Vol. 89, pages 885-889, see entire document.	1-54
A	YAMADA et. al. In Vivo Identification of a Negative Regulatory Element in the Mouse Renin Gene using Direct Gene Transfer. Journal of Clinical Investigation. September 1996, Vol. 96, pages 1230-1237, see entire document.	1-54

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
20 JULY 1999	18 AUG 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer THOMAS G. LARSON, PH.D. Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/08502

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T,E	TOMITA et al. Transcription Factor Decoy to Study the Molecular Mechanism of Regulation of Renin Gene Expression in the Liver In Vivo. Circulation Research. 14 May 1999, pages 1059-1066, see entire document.	22-38

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/08502

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-54

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/08502

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

A61K 31/70, 38/17, 39/00; C07H 21/00, 21/04; C12N 5/06, 5/16, 15/85; C12Q 1/68

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

435/6, 320.1, 325, 375; 530/300, 350; 514/2, 44; 536/23.5, 24.31, 24.5

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-21, drawn to a nucleic acid encoding the CNREB-2 protein, the CNREB-2 protein, and a method of isolating nucleic acids encoding the CNREB-2 protein.

Group II, claim(s) 22-38, drawn to methods of using CNREB-1 inhibitors to decrease renin expression in a cell or in a subject.

Group III, claim(s) 39-54, drawn to methods of using a CNREB-1 activator to increase CNREB-1 activity in a cell or subject.

Group IV, claims 55-60, drawn to a method of determining CNREB-1 expression levels in a subject.

Group V, claims 61-79, drawn to a method of testing for alterations in the CNREB-1 sequence as a means of determining a subject's susceptibility to a renin-angiotensin mediated disorder.

Group VI, claims 80-84, drawn to a method of modulating c-myc expression by modulating CNREB-1 expression.

Group VII, claims 85-89, drawn to a method of modulating collagen type II expression by modulating CNREB-1 expression.

Group VIII, claims 90-94, drawn to a method of modulating T cell receptor expression by modulating CNREB-1 expression.

Group IX, claims 95-98, drawn to a pharmaceutical composition comprising a CNREB-1 inhibitor.

The inventions listed as Groups I-IX do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Under Rule 13 there is unity of invention between an independent claim for a composition, an independent claim for preparing a composition, and an independent claim for using the composition. Group I contains an independent claim to the nucleic acids encoding CNREB-2 protein and an independent claim to a method of isolating the nucleic acid encoding CNREB-2 protein. The remaining groups are drawn to methods relating to the CNREB-1 protein and its expression or to a composition comprising an inhibitor of the CNREB-1 protein The CNREB-1 and CNREB-2 proteins appear to be distinct compositions so that there is no common special technical feature linking the methods related to the CNREB-1 protein to the compositions related to the CNREB-2 protein. Therefore, the claims of groups I-IX do not relate to a single inventive concept under PCT Rule 13.